Original Report: Patient-Oriented, Translational Research

American Journal of Nephrology

Am J Nephrol 2013;37:59–64
DOI: 10.1159/000346206

Received: July 14, 2012
Accepted: November 30, 2012
Published online: January 11, 2013

Dysnatremias and Survival in Adult Burn Patients: A Retrospective Analysis

Ian J. Stewart[a] Benjamin D. Morrow[a] Molly A. Tilley[a] Brian D. Snow[a] Christopher Gisler[b] Keith W. Kramer[a] James K. Aden[c] Evan M. Renz[c, d] Kevin K. Chung[c, d]

[a]San Antonio Military Medical Center, Fort Sam Houston, Tex., [b]San Antonio Kidney Disease Center, San Antonio, Tex., [c]United States Army Institute of Surgical Research, Fort Sam Houston, Tex., and [d]Uniformed Services University of the Health Sciences, Bethesda, Md., USA

Key Words
Acute kidney injury · Burn · Dysnatremia · Hypernatremia · Hyponatremia · Mortality

Abstract
Background/Aims: Dysnatremias have been evaluated in many populations and have been found to be significantly associated with mortality. However, this relationship has not been well described in the burn population. ***Methods:*** Admissions to the burn center at our institution from January 2003 to December 2008 were examined. Independent variables included gender, age, percentage total body surface area burned (%TBSA), percentage of third-degree burn, inhalation injury, injury severity score (ISS), Acute Kidney Injury Network (AKIN) stage, hypernatremia, and hyponatremia. They were examined via Cox proportional hazard regression models against death. Moderate to severe hypo- and hypernatremia were defined as serum sodium <130 and >150 mmol/l, respectively. ***Results:*** In 1,969 subjects with a mean age of 36.3 ± 16.4 years, a median %TBSA of 9 (interquartile range 4–20) and a median ISS of 5 (interquartile range 1–16) hypernatremia occurred in 9.9% (n = 194), while hyponatremia occurred in 6.8% (n = 134) with mortality rates of 33.5 and 13.8%, respectively. Patients without a dysnatremia had a mortality rate of 4.3%. On Cox proportional hazard regression age, %TBSA, ISS, and AKIN stage were found to be significant predictors of mortality. Hypernatremia (HR 2.00, 95% CI 1.212–3.31; p = 0.0066), but not hyponatremia (HR 1.72, 95% CI 0.89–3.34; p = 0.1068) was associated with mortality. ***Conclusions:*** In the burn population, hypernatremia, but not hyponatremia, is an independent predictor of mortality.

Introduction

Both hypernatremia [1–4] and hyponatremia [1, 4, 5] have been examined in the hospital setting and have been found to be significantly associated with mortality. Hyponatremia has been observed in 14.5–37.9% of patients upon hospital admission [1, 5–7], while rates for hospital-acquired hyponatremia range from 11 to 38.2% [4, 5, 8]. Mortality rates vary significantly based on the population studied, and in several studies hyponatremia has been associated with an increased risk of death [1, 4, 5, 7, 8]. The incidence of hypernatremia has been reported to be 2–9% upon hospital admission [1, 2]. After admission to an intensive care unit (ICU), patients developed hyper-

KARGER

Fax +41 61 306 12 34
E-Mail karger@karger.com
www.karger.com

Accessible online at:
www.karger.com/ajn

Ian J. Stewart, MD
San Antonio Military Medical Center, ATTN: Nephrology
3551 Roger Brooke Drive
Fort Sam Houston, TX 78234 (USA)
E-Mail ian.stewart@amedd.army.mil

Report Documentation Page

Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
01 JAN 2013	**N/A**	**-**

4. TITLE AND SUBTITLE	5a. CONTRACT NUMBER
Dysnatremias and Survival in Adult Burn Patients: A Retrospective Analysis	5b. GRANT NUMBER
	5c. PROGRAM ELEMENT NUMBER
6. AUTHOR(S)	5d. PROJECT NUMBER
Stewart I. J., Morrow B. D., Tilley M. A., Snow B. D., Gisler C., Kramer K. W., Aden J. K., Renz E. M., Chung K. K.,	5e. TASK NUMBER
	5f. WORK UNIT NUMBER
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)	8. PERFORMING ORGANIZATION REPORT NUMBER
United States Army Institute ofSurgical Research, JBSA Fort Sam Houston, TX	
9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)	10. SPONSOR/MONITOR'S ACRONYM(S)
	11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION/AVAILABILITY STATEMENT
Approved for public release, distribution unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

15. SUBJECT TERMS

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			
unclassified	**unclassified**	**unclassified**	**UU**	**6**	

natremia at rates of 7–26% [3, 8]. In these cohorts, hypernatremia was significantly associated with mortality [1–3, 8].

In the burn population, hypernatremia has not been well studied. In the small studies done to date, the incidence of hypernatremia is seemingly higher than other populations at 34–37.5% and has been associated with mortality [9, 10]. Hyperosmolarity is associated with peripheral insulin resistance [11] and decreased myocardial contractility [12] which could thus result in poor outcomes.

To our knowledge, the incidence of hyponatremia and its possible association with mortality has not been evaluated in the setting of burn injuries. We sought to evaluate the incidence and mortality risk associated with sodium disorders in patients with burn injuries admitted to our institution.

Methods

After approval from the institutional review board, we retrospectively reviewed all admissions to our burn center from January 2003 to November 2008. Patients were included for analysis if they were aged >18 years, were admitted for >24 h and had a serum sodium level obtained in their hospital course. Patients were excluded from analysis if they had end-stage renal disease prior to admission, or did not have burn or inhalation injury.

Data were obtained by review of the electronic medical record and by search of a prospectively collected trauma registry. Age, sex, percentage of total body surface area burned (%TBSA), percentage of full-thickness burn (%FT), injury severity score (ISS), days on mechanical ventilation, days in the ICU, days in the hospital, presence of inhalation injury, electrical burn, renal replacement therapy (RRT), and mortality were recorded from these sources. The ISS is a validated method for describing patients with multiple traumatic injuries [13]. Acute kidney injury (AKI) was diagnosed by the AKI network (AKIN) criteria [14]. Since we did not have access to a known baseline creatinine, the lowest creatinine obtained in the first 7 days of hospitalization was used as a surrogate. If a patient had only one creatinine measured in the first 7 days or if the creatinine increased over the first 7 days, a baseline creatinine was estimated by solving the Modification of Diet in Renal Disease (MDRD) study equation assuming an estimated glomerular filtration rate of 75 ml/min/1.73 m^2. For example, if a patient was admitted with a serum creatinine level of 2 mg/dl and it progressively increased to 4 mg/dl over the course of 7 days, the MDRD equation was used to determine a baseline instead of using the lowest value in the first 7 days (which for this case would be 2 mg/dl). Our study was limited to moderate to severe hypo- and hypernatremia, which were defined as <130 and >150 mmol/l, respectively.

Statistical analysis was performed using SAS version 9.2 (Cary, N.C., USA). Categorical variables from each group were compared via χ^2 analysis, whereas continuous variables were compared via a Student t test as appropriate.

Table 1. Characteristics of the patient cohort

Variable	Patients (n = 1,969)
Mean age ± SD, years	36 ± 16
Male, n (%)	1,701 (86)
Median %TBSA (IQR)	9 (4–20)
Median %FT TBSA (IQR)	0 (0–5)
Median ISS (IQR)	5 (1–16)
Inhalation injury, n (%)	250 (13)
Electrical burn, n (%)	103 (5)
Acute kidney injury, n (%)	
AKIN-1	435 (22.1)
AKIN-2	73 (3.7)
AKIN-3	146 (7.4)
Hypernatremia, n (%)	194 (9.9)
Hyponatremia, n (%)	134 (6.8)
Median first day of hyponatremia (IQR)	6.5 (2–21)
Median duration of hyponatremia (IQR), days	2 (1–3)
Median day of hypernatremia (IQR)	7.5 (5–12)
Median duration of hypernatremia (IQR), days	4 (2–9)

A multiple logistic regression analysis was performed to analyze the relationship between independent variables of age, gender, %TBSA, %FT, inhalation injury, ISS, electrical burn, and AKI against the dependent variables of hypo- and hypernatremia. Factors that were deemed insignificant ($p > 0.1$) were removed from the model via backwards elimination. Survival times and the first day of dysnatremia within 60 days were used in a Cox proportional hazard regression model along with age, ISS, %TBSA, and AKIN stage (as a continuous variable). Survival time was defined as the time between admission to the burn unit and death. All patients who left the ICU alive within 60 days were considered to have survived beyond 60 days. Patients who remained in the ICU for longer than 60 days were censored at day 60. Hyper- and hyponatremia were evaluated in the models as time-dependent prognostic variables such that patients were reclassified into the hyper- or hyponatremic group on the day the dysnatremia was first acquired, then remained in that group whether or not the dysnatremia resolved or multiple dysnatremic episodes occurred.

Results

Our initial search was for patients who were >18 years of age, admitted for >24 h and had serum creatinine measured at some point in their hospitalization. This yielded 1,973 patients, of whom 4 did not have serum sodium checked. This resulted in 1,969 patients for analysis. Characteristics of the patient cohort are described in table 1. Males comprised 86% of the cohort, and the average age (±SD) was 36 ± 16 years. Median (with interquartile (IQR) ranges) for %TBSA, %FT, and ISS were 9 (4–20), 0

Table 2. Characteristics of patient cohort stratified by nadir and peak sodium levels

Variable	Peak sodium			Nadir sodium		
	≤150	>150	p value	≥130	<130	p value
Mean age ± SD, years	36 ± 16	37 ± 17	0.78	36 ± 16	36 ± 18	0.93
Male, %	86.1	89.2	0.24	86.3	88.4	0.48
Median %TBSA (IQR)	8 (4–16)	45 (30–58)	<0.0001	8 (4–18)	26 (17–44)	<0.0001
Median %FT (IQR)	0 (0–2)	28 (9–48)	<0.0001	0 (0–3)	14 (3–31)	<0.0001
Median ISS (IQR)	4 (1–9)	25 (25–34)	<0.0001	4 (1–12)	20 (9–27)	<0.0001
Inhalation injury, %	9.2	44.3	<0.0001	12.2	18.8	0.0239
Electrical burn, %	7.7	4.4	0.1095	7.1	8.3	0.6650
AKI, %			<0.0001			<0.0001
AKIN-1	20.5	36.1		20.4	43.5	
AKIN-2	2.8	10.8		3.2	8.7	
AKIN-3	3.4	47.4		6.5	23.2	
Median ventilator days (IQR)	0 (0–1)	16 (5–39)	<0.0001	0 (0–2)	3 (0–10)	0.0003
Median ICU days (IQR)	0 (0–3)	35 (15–65)	<0.0001	0 (0–4)	11 (3–32)	<0.0001
Median hospital days (IQR)	6 (2–15)	63 (34–100)	<0.0001	7 (3–17)	42 (18–72)	<0.0001
RRT, %	1.4	28.9	<0.0001	3.4	13.0	<0.0001
Mortality, %	4.5	33.5	<0.0001	6.9	13.8	0.0027

(0–5), and 5 (1–16), respectively. Inhalation injury was diagnosed in 13% and electrical burn was noted in 5% of patients. The incidence of hyponatremia was 6.8% (n = 134) and for hypernatremia it was 9.9% (n = 194). The mean nadir sodium for patients with hyponatremia was 128 ± 2 mmol/l, whereas the mean peak sodium for patients with hypernatremia was 155 ± 4 mmol/l. The median first day of hyper- and hyponatremia was 7.5 (5–12) and 6.5 (2–21), respectively. The median duration of hypernatremia was 4 days (2–9) and 2 days (1–3) for hyponatremia. The rates of AKI in this cohort has been previously described [15]. Of the 194 patients with hypernatremia, only 6 had concurrent head trauma for which an elevated sodium level was recommended by neurosurgery.

When stratified by the presence of hyper- and hyponatremia, differences between the groups were observed (table 2). Patients with a peak sodium >150 were more acutely ill as evidenced by significantly higher burn sizes, higher ISS, more inhalation injury, and more AKI. Patients with hypernatremia also had significantly more days on mechanical ventilation, days in the ICU, and days in the hospital. Similar differences were noted in patients with a nadir sodium <130. On multivariate analysis, the subsequent development of hypernatremia was significantly associated with ISS (odds ratio (OR) 1.04, 95% confidence interval (CI) 1.02–1.06; p = 0.0004), days spent on mechanical ventilation (OR 1.06, 95% CI 1.05–1.08; p < 0.0001), %TBSA (OR 1.02, 95% CI 1.01–1.03; p = 0.0034), AKIN-1 (OR 6.88, 95% CI 3.41–13.86; p < 0.0001), AKIN-2 (OR 9.04, 95% CI 3.67–22.15; p < 0.0001), and AKIN-3 (OR 15.29, 95% CI 6.86–34.07; p < 0.0001). Hyponatremia was associated with inhalation injury (OR 0.45, 95% CI 0.27–0.75; p = 0.0025), %TBSA (OR 1.02, 95% CI 1.01–1.03; p < 0.0001), AKIN-1 (OR 5.42, 95% CI 3.33–8.83; p < 0.0001), AKIN-2 (OR 6.23, 95% CI 2.90–13.40; p < 0.0001), and AKIN-3 (OR 6.54, 95% CI 3.38–12.65; p < 0.0001).

Table 3. Cox proportional hazard regression model with hyponatremia for mortality

Variable	HR (95% CI) for hospital mortality	p value
Age	1.07 (1.05–1.08)	<0.0001
%TBSA	1.04 (1.03–1.06)	<0.0001
ISS	1.03 (1.02–1.05)	0.0001
AKIN stage	1.56 (1.29–1.88)	<0.0001
Hyponatremia	1.72 (0.89–3.34)	0.1068

HRs for age, TBSA and ISS reflect per year increase in age, per 1% increase in TBSA and per 1 point increase in ISS, respectively. HR for AKIN denotes per increase in AKIN stage (e.g. AKIN-0 to AKIN-1, AKIN-1 to AKIN-2).

Table 4. Cox proportional hazard regression model with hypernatremia for mortality

Variable	HR (95% CI) for hospital mortality	p value
Age	1.07 (1.06–1.08)	<0.0001
%TBSA	1.04 (1.03–1.06)	<0.0001
ISS	1.03 (1.02–1.05)	0.0002
AKIN stage	1.48 (1.23–1.80)	<0.0001
Hypernatremia	2.00 (1.21–3.31)	0.0066

HRs for age, TBSA and ISS reflect per year increase in age, per 1% increase in TBSA and per 1 point increase in ISS, respectively. HR for AKIN denotes per increase in AKIN stage (e.g. AKIN-0 to AKIN-1, AKIN-1 to AKIN-2).

The Cox proportional hazard regression models are presented in tables 3 and 4. The factors found to be associated with mortality in the model for hyponatremia were ISS (hazard ratio (HR) 1.03, 95% CI 1.02–1.05; p = 0.0001), age (HR 1.07, 95% CI 1.05–1.08; p < 0.0001), %TBSA (HR 1.04, 95% CI 1.03–1.06; p < 0.0001), and AKIN stage (HR 1.56, 95% CI 1.29–1.88; p < 0.0001). The development of hyponatremia was not significant (HR 1.72, 95% CI 0.89–3.34; p = 0.1068). ISS, age and %TBSA were also significant in the model for hypernatremia. However, in this model the development of hypernatremia was significantly associated with mortality (HR 2.00, 95% CI 1.21–3.31; p = 0.0066).

We found that on univariate analysis, mortality was higher in both the hypernatremia (33.5%) and hyponatremia (13.8%) groups compared to patients without a dysnatremia (4.3%). However, in the Cox regression analysis, only hypernatremia was associated with mortality. To investigate why hyponatremia was no longer significant, we examined other variables in the Cox regression analysis that could account for this and found that AKI uniquely emphasized this effect. When we removed AKI from the analysis, we found that hyponatremia became significant for mortality (HR 1.95, 95% CI 1.004–3.77; p = 0.0485).

Discussion

We found that hyper- and hyponatremia were present in 9.9 and 6.8%, respectively, of patients admitted to our burn unit. While mortality was significantly higher for both disorders on univariate analysis, only hypernatremia was significant after adjustment. Our study is the largest to date in the burn population. To our knowledge, this is the first time, in any population, that the effect of the dysnatremias on mortality has been examined in a multivariate model with the AKIN criteria. In order to eliminate the risk of immortal time bias, we used a Cox proportional hazards model which treats ICU-acquired dysnatremias as time-dependent prognostic factors.

Our study is the first to systematically examine the prevalence of hyponatremia in a population of burned patients. The prevalence of 6.8% found in the present study is congruent with prior estimates, using a definition of <130 mmol/l, of 3.9–14.5% in other patient populations [1, 7, 16, 17]. In contradistinction to prior work however, we did not find a significant association of hyponatremia with mortality after adjustment. Our method has distinct differences from prior studies. Since regulation of water balance by the kidneys is related to renal function, adjustment for AKI, which is well known to be associated with mortality, particularly in the burn population [18], is imperative. A strength of the present analysis is that we used the AKIN criteria [14] for this purpose. Other work has used different methods to account for renal dysfunction. One study that found an association of hyponatremia with mortality in hospitalized patients with cancer used the mean serum creatinine [16]. Another study of hospitalized patients that found an association of hyponatremia with both in-hospital death and death after discharge used ICD-9 codes to adjust for kidney disease [17]. Other work that has demonstrated an association of hyponatremia with mortality has accounted for AKI indirectly with the Simplified Acute Physiology Score II [1] (in a population of ICU patients with hyponatremia on admission), or the Acute Physiology and Chronic Health Evaluation II score [4, 8, 19] (in populations following cardiac surgery, general medical patients and ICU patients). Another study of patients with community- and hospital-acquired hyponatremia used the Deyo-Charlson Comorbidity Index and also stratified patients on the basis of chronic kidney disease [5]. Our results demonstrate the importance of adjusting for AKI because when we removed it from the model, hyponatremia became significant for mortality. This raises the possibility that had prior work accounted for AKI, they might not have seen a correlation between hyponatremia and mortality. To our knowledge, this multivariate analysis is the first to use the well-validated AKIN criteria in this setting.

It has been suggested that the association of hyponatremia with mortality is not causal [6]. Chawla et al. [6] found that while moderate hyponatremia was associated with mortality, severe hyponatremia (serum sodium <110 mmol/l) was not. The majority of patients with a

nadir sodium of <110 mmol/l were admitted for hyponatremia and were not severely ill. When the causes of death were examined, all patients who died had severe progressive underlying illness. After chart review, these authors could plausibly associate only 3 deaths to hyponatremia. Taken together, they concluded that hyponatremia is more likely to be a marker of illness rather than having a casual effect on mortality. Our findings, in a homogeneous population of burn patients with a rigorous multivariate model, serve to confirm these results.

We found that 9.9% of admissions were associated with hypernatremia, an incidence similar to prior estimates of 1.3–9% in other populations using a similar definition of hypernatremia [1–3, 20–23]. The wide range in these estimates is a reflection of the different populations studied. Increased insensible losses resulting from burn injury are recognized to cause hypernatremia, and there are several small studies specific to this population. In a study by Ebrahim et al. [9] of 105 patients with burn injury and septicemia, 34% were found to have hypernatremia (defined as serum sodium >150 mmol/l). Congruent with our findings on univariate analysis, patients with hypernatremia had larger %TBSA and more inhalation injury. However, they also demonstrated that patients with hypernatremia were older and more likely to be female, associations which we did not demonstrate. Another study of 40 patients with %TBSA >10% found that the incidence of hypernatremia (defined by serum sodium ≥146 mmol/l) was 37.5% [10]. Limiting our study to patients with >10% TBSA (n = 893) and changing the definition of hypernatremia to ≥146 mmol/l, we found a similar incidence (35.4%). The Ebrahim study was not sufficiently powered to assess variables associated with hypernatremia, but they did note a higher creatinine (89 vs. 72 μmol/l) in the hypernatremic group. The mortality rate was noted to be 20% in the hypernatremic group compared with 0% in the eunatremic group ($p = 0.046$). Using a sodium cutoff of ≥146 mmol/l and limiting our analysis to >10% TBSA, we found mortality rates of 30.7 and 6.4% in the hyper- and eunatremic groups, respectively. While prior work in the burn population has suffered from low numbers of patients examined, our work is the first to show a correlation of hypernatremia with mortality after adjustment.

Similar to prior work, we found that, after adjustment, hypernatremia was significantly associated with mortality. Our study serves to confirm these findings and places them, for the first time, in a multivariate model with the well-validated AKIN criteria. Other multivariate analyses demonstrating an association of hypernatremia with mortality have used different methods for correcting for renal function. One study examined the Simplified Acute Physiology Score II and the Logistic Organ Dysfunction score at admission [21]. While this study accounted for chronic kidney disease at admission, the only variable that included AKI during the hospital course was the need for RRT. Other studies have examined renal dysfunction indirectly and at a single point in time using the Simplified Acute Physiology Score II [1, 2, 24], the Acute Physiology and Chronic Health Evaluation II score [3, 4, 8, 19], or the EUROSCORE [24]. One study examined renal dysfunction defined by creatinine ≥100 μmol/l for females or ≥125 μmol/l for males [25], whereas another study examined chronic kidney disease, RRT, and a creatinine ≥200 μmol/l [3]. We are unaware of any studies using the AKIN criteria in a model with hypernatremia for the outcome of mortality.

Our study has a variety of limitations. First, it is a retrospective analysis and as such is subject to the limitations inherent in that form of study. The classification of AKIN stage was limited by our lack of a known baseline serum creatinine and data on urine output. We also did not correct for glucose, which can affect sodium levels. However, the practice in our institution is to maintain the glucose between 100 and 150 mg/dl, which would minimize this effect. It is also important to note that the results in burn patients may not be generalizable to other populations. Furthermore, a portion of our cohort (35%) were casualties from the wars in Iraq and Afghanistan. These were predominantly males (97%) and had different patterns of injury than that seen in civilian centers.

In conclusion, we found that hypernatremia, but not hyponatremia, was correlated with mortality in a population of burn patients after adjustment. As we found that AKIN stage was significantly associated with the development of both dysnatremias and mortality, adjustment for AKI should be included in future analyses.

Acknowledgement

We would like to thank Otilia Sánchez for editing and formatting of the manuscript.

Disclosure Statement

The authors have no potential conflicts of interest to declare. The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the Department of the Army, the Department of the Air Force, or the Department of Defense.

References

1 Funk GC, Lindner G, Druml W, et al: Incidence and prognosis of dysnatremias present on ICU admission. Intensive Care Med 2010; 36:304–311.

2 Lindner G, Funk GC, Schwarz C, et al: Hypernatremia in the critically ill is an independent risk factor for mortality. Am J Kidney Dis 2007;50:952–957.

3 O'Donoghue SD, Dulhunty JM, Bandeshe HK, Senthuran S, Gowardman JR: Acquired hypernatraemia is an independent predictor of mortality in critically ill patients. Anaesthesia 2009;64:514–520.

4 Stelfox HT, Ahmed SB, Zygun D, Khandwala F, Laupland K: Characterization of intensive care unit acquired hyponatremia and hypernatremia following cardiac surgery. Can J Anaesth 2010;57:650–658.

5 Wald R, Jaber BL, Price LL, Upadhyay A, Madias NE: Impact of hospital-associated hyponatremia on selected outcomes. Arch Intern Med 2010;170:294–302.

6 Chawla A, Sterns RH, Nigwekar SU, Cappuccio JD: Mortality and serum sodium: do patients die from or with hyponatremia? Clin J Am Soc Nephrol 2011;6:960–965.

7 Waikar SS, Mount DB, Curhan GC: Mortality after hospitalization with mild, moderate, and severe hyponatremia. Am J Med 2009;122:857–865.

8 Stelfox HT, Ahmed SB, Khandwala F, Zygun D, Shahpori R, Laupland K: The epidemiology of intensive care unit-acquired hyponatraemia and hypernatraemia in medical-surgical intensive care units. Crit Care 2008; 12:R162.

9 Ebrahim MK, George A, Bang RL: Only some septicaemic patients develop hypernatremia in the burn intensive care unit: why? Burns 2002;28:543–547.

10 Namdar T, Siemers F, Stollwerck PL, Stang FH, Mailander P, Lange T: Increased mortality in hypernatremic burned patients. Ger Med Sci 2010;8:Doc11.

11 Bratusch-Marrain PR, DeFronzo RA: Impairment of insulin-mediated glucose metabolism by hyperosmolality in man. Diabetes 1983;32:1028–1034.

12 Kozeny GA, Murdock DK, Euler DE, et al: In vivo effects of acute changes in osmolality and sodium concentration on myocardial contractility. Am Heart J 1985;109:290–296.

13 Baker SP, O'Neill B, Haddon W Jr, Long WB: The injury severity score: a method for describing patients with multiple injuries and evaluating emergency care. J Trauma 1974; 14:187–196.

14 Mehta RL, Kellum JA, Shah SV, et al: Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury. Crit Care 2007;11:R31.

15 Chung KK, Stewart IJ, Gisler C, et al: The Acute Kidney Injury Network (AKIN) criteria applied in burns. J Burn Care Res 2012;33: 483–490.

16 Doshi SM, Shah P, Lei X, Lahoti A, Salahudeen AK: Hyponatremia in hospitalized cancer patients and its impact on clinical outcomes. Am J Kidney Dis 2012;59:222–228.

17 Tierney WM, Martin DK, Greenlee MC, Zerbe RL, McDonald CJ: The prognosis of hyponatremia at hospital admission. J Gen Intern Med 1986;1:380–385.

18 Brusselaers N, Monstrey S, Colpaert K, Decruyenaere J, Blot SI, Hoste EA: Outcome of acute kidney injury in severe burns: a systematic review and meta-analysis. Intensive Care Med 2010;36:915–925.

19 Whelan B, Bennett K, O'Riordan D, Silke B: Serum sodium as a risk factor for in-hospital mortality in acute unselected general medical patients. QJM 2009;102:175–182.

20 Adams D, de Jonge R, van der Cammen T, Zietse R, Hoorn EJ: Acute kidney injury in patients presenting with hyponatremia. J Nephrol 2011;24:749–755.

21 Darmon M, Timsit JF, Francais A, et al: Association between hypernatraemia acquired in the ICU and mortality: a cohort study. Nephrol Dial Transplant 2010;25:2510–2515.

22 Palevsky PM, Bhagrath R, Greenberg A: Hypernatremia in hospitalized patients. Ann Intern Med 1996;124:197–203.

23 Polderman KH, Schreuder WO, Strack van Schijndel RJ, Thijs LG: Hypernatremia in the intensive care unit: an indicator of quality of care? Crit Care Med 1999;27:1105–1108.

24 Lindner G, Funk GC, Lassnigg A, et al: Intensive care-acquired hypernatremia after major cardiothoracic surgery is associated with increased mortality. Intensive Care Med 2010;36:1718–1723.

25 Hoorn EJ, Betjes MG, Weigel J, Zietse R: Hypernatraemia in critically ill patients: too little water and too much salt. Nephrol Dial Transplant 2008;23:1562–1568.